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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/042,991	01/09/2002	Ian Michael Whitehead	06027.0001U3	7697

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EXAMINER
HUTSON, RICHARD G

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/042,991	WHITEHEAD ET AL.	
	Examiner	Art Unit	
	Richard G Hutson	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 March 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-15 are at issue and are present for examination.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1, 3, 4, 6, 7, 9, 10, 12, 13 and 15, and SEQ ID NO: 1, claims 1-3, in Paper No. 6 is acknowledged. The traversal is on the ground(s) that it would not be a serious burden to search and examine Groups I and II together, per M.P.E.P. 803. The restriction between groups I and II is hereby withdrawn based on that the methods of Groups I and II are each drawn to the same enzymatic reaction, generating a C_6-aldehyde, merely different in the specification of the generated product.

With respect to SEQ ID NOs: 1-4 and 6, it is pointed out to applicants that a restriction requirement was made between the different SEQ ID NOs: 1-4 and 6, not an election of species, however, in light of the significant overlap between the SEQ ID NOs: 1-4 and 6, this restriction requirement has been removed and the methods of Group I comprising the use of any of SEQ ID NOs: 1-4 and 6 will be examined.

Priority

Applicants statement on the first line of the specification that this application is a divisional of and claims the benefit of U.S. Serial No. 09/578,533, filed May 24, 2000, which is a pending application and which claims priority to U.S. Serial No. 09/078,173,

filed May 13, 1998, which has issued as U.S. Patent No. 6,200, 794, both of which are incorporated herein by reference in their entirety, is acknowledged.

Information Disclosure Statement

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609 A(1) states, "the list may not be incorporated into the specification but must be submitted in a separate paper."

Applicants filing of information disclosures, Paper No. 3, filed 4/17/2002, is acknowledged. Those references considered have been initialed.

Specification

The disclosure is objected to because of the following informalities:

The figures contain Figure 1A, 1B, 2A and 2B, while the Description of the Figures merely refers to Figure 1 and Figure 2. It is suggested that the description of the figures be amended to describe Figure 1A and 1B and Figure 2A and 2B.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1-15 are indefinite in the recitation of "fatty acid 13-hydroperoxide lyase" as the specification defines a "fatty acid 13-hydroperoxide lyase" as a lyase protein having at least one function exhibited by native 13-hydroperoxide lyase, including catalytic activity as well as antigenic activity (see specification, page 5, lines 21-30). This definition of what applicants consider to be encompassed by the term "fatty acid 13-hydroperoxide lyase" is contrary to that which one of skill in the art would consider to be encompassed by the term. The ordinary artisan would consider a "fatty acid 13-hydroperoxide lyase" to have at the minimum enzymatic or catalytic activity, which as defined by the specification is not essential for the described protein, only an option.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3 are directed to all possible methods of cleaving a 13-hydroperoxide or a α-linolenic acid into C_6-aldehyde and a C_{12}-oxocarboxylic acid comprising contacting

the 13-hydroperoxide with a recombinant protein comprising any fatty acid lyase (see above 112 second paragraph rejection) comprising the amino acid sequence set forth in SEQ ID NO: 1.

The specification, however, only provides the representative species of the claimed methods of use of SEQ ID NOs: 2, 3, 4 and 6, encompassed by the claimed genus. There is no disclosure of any particular structure to function/activity relationship in the disclosed species. The specification also fails to describe additional representative species of the polypeptides necessary for the claimed methods by any identifying structural characteristics or properties for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those claimed methods of use of a 13-hydroperoxide lyase enzyme wherein said polypeptide comprises the amino acid sequence of SEQ ID NOs: 2, 3, 4, or 6, does not reasonably provide enablement for those claimed methods of use of a 13-hydroperoxide lyase enzyme wherein said

polypeptide merely comprises SEQ ID NO: 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 1-3 are so broad as to encompass the claimed methods of use of any "fatty acid 13-hydroperoxide lyase" comprising SEQ ID NO: 1. SEQ ID NO: 1 is a 7 amino acid fragment of an approximately 480 amino acid protein. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the methods of use of the extremely large number of enzymes broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to those methods of use of those

polypeptides having 13-hydroperoxide lyase enzymatic activity wherein said polypeptide comprises the amino acid sequence of SEQ ID NOs: 2, 3, 4, or 6.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass those methods of use of any polypeptide mutant or fragment of any 13-hydroperoxide lyase comprising SEQ ID NOs: 1, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting 13-hydroperoxide lyase enzymatic activity; (B) the general tolerance of 13-hydroperoxide lyases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the 13-hydroperoxide lyase activity necessary to practice the claimed methods and the fact that

the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to arrive at the majority of those polypeptides having the necessary 13-hydroperoxide lyase activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any 13-hydroperoxide lyase, so long as the polypeptide comprises SEQ ID NOs: 1. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those polypeptides having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Remarks

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G Hutson whose telephone number is (703) 308-0066. The examiner can normally be reached on 7:30 am to 4:00 pm, M-F.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on (703) 308-3804. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 305-3014 for regular communications and (703) 305-3014 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Richard G Hutson, Ph.D.
Primary Examiner
Art Unit 1652

rgh
May 19, 2003